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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,852	11/07/2001	Alan M. Kinnersley	7224-65	8960

7590 11/20/2003

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/006,852	KINNERSLEY ET AL.	
	Examin r	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *16-18,21,24,25,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,19,20,22,23,26-28 and 31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-15, 19-20, 22-23, 26-28, and 31-34, and Group (A), SEQ ID NOS: 1 and 2, in the response filed August 21, 2003, is acknowledged. The traversal is on the ground(s) that it would not be unduly burdensome to search both Groups I and II because the subject matter overlaps. This is not found persuasive because while the subject matter of Groups I and II may overlap, a search of the two groups is not coextensive. Specifically, a search of Group II requires a search of all cell types from all groups of organisms, both prokaryotic and eukaryotic, whereas a search of Group I requires a search of plant cells only.

The traversal is also on the ground(s) that each of the restricted sequences is a species of a properly defined genus related to one another in both structure and function. This is not found persuasive because nucleotide sequences encoding different amino acid sequences are deemed to constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. That the restricted sequences have common structural and functional features does not rebut this presumption, as the search of the prior art indicates that the restricted sequences also exhibit structural and functional differences. Absent the assertion that the restricted sequences are not patentably distinct, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

The requirement is still deemed proper and is therefore made FINAL. Claims 16-18, 21, 24-25, 29-30, and the nonelected sequences, are withdrawn from consideration as being directed to nonelected inventions.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed December 2, 2002 is attached to the instant Office action.

Claim Objections

Claims 8, 12, 28, 35 and 40 are objected to because they recite nonelected sequences. Appropriate correction is required.

Claims 19, 20, 22 and 26 are objected to because they depend from claims withdrawn from consideration as being directed to nonelected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15, 19-20, 22-23, 26-28 and 31-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to methods for making transformed plants that comprise transforming a plant with a DNA construct comprising any non-constitutive or

constitutive promoter operably linked to a polynucleotide encoding any functional GAD enzyme of undefined structure obtained from any plant species, including a modified GAD enzyme that does not include a functional autoinhibitory calmodulin-binding domain, including a GAD enzyme comprising any amino acid sequence having at least about 60% identity to SEQ ID NO:2, and including any polynucleotide that hybridizes under moderately stringent conditions to SEQ ID NO:1, and to constructs and plants comprising said polynucleotides.

In contrast, the specification describes only nine specific sequences obtained from four different species of dicotyledonous plants (*Arabidopsis*, tobacco, petunia and tomato) that are said to correspond to GAD enzymes. Additionally, the specification does not describe the extent to which, if any, these sequences are structurally and functionally related to one another. Accordingly, polynucleotides that encode any functional GAD enzyme of undefined structure obtained from any plant species are not adequately described, as a representative number of species that would support the description of such a broad genus are not disclosed.

Additionally, the specification does not describe the structural characteristics of a modified GAD enzyme that does not include a functional autoinhibitory calmodulin-binding domain, even though the prior art indicates that specific but variable structural characteristics as associated with the calmodulin-binding domain of plant GAD enzymes. For example, Turano et al. teach that the calmodulin-binding domain of plant GAD enzymes located in the highly variable carboxyterminal region of GAD, and that the calmodulin-binding domain itself varies between different GAD sequences (Plant Physiology, 1998, Vol. 117, pages 1411-1421, see page 1419 column 1 second full

paragraph; page 1415 paragraph column 2). In light of the varibility of plant GAD calmodulin-binding domains, modified GAD enzymes that do not include a functional autoinhibitory calmodulin-binding domain are not described.

Furthermore, the specification does not describe the structural characteristics of SEQ ID NO:2 that are retained by functional plant GAD enzymes having at least about 60% identity to SEQ ID NO:2, or the structural characteristics of SEQ ID NO:1 that are retained by polynucleotides that encode functional plant GAD enzymes and that hybridize to SEQ ID NO:1 under moderately stringent conditions, even though the prior art indicates that specific structural characteristics as associated with functional plant GAD enzymes. For example, Turano et al. teach that GAD peptides are divided into 3 distinct regions: (1) a small amino terminal variable region of unknown functional significance, (2) a large highly conserved middle region encoding GAD enyzmatic acitvity, and (3) a small carboxy terminal variable region encoding the calmodulin binding domain (Plant Physiology, 1998, Vol. 117, pages 1411-1421, see page 1419 column 1 second full paragraph). Turano et al. teach also that the *Arabidopsis* GAD1 and GAD2 sequences comprise a Ser-X-X-Lys amino acid motif common among PLP-requiring enzymes, and that the Ser-X-X-Lys motif is conserved in both identity and position as compared to GAD enzymes of petunia, tomato, and the *gadA* and *gadB* genes of *E. coli* (see paragraph spanning columns 1 and 2 page 1415; page 1419 column 1 second full paragraph). In light of GAD's requirement for specific structural characteristics, amino acid sequences having at least about 60% identity to SEQ ID NO:2 that correspond to functional plant GAD enzymes are not described. Likewise,

polynucleotides that hybridize to SEQ ID NO:1 under moderately stringent conditions and that encode functional plant GAD enzymes are not described.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lily and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Given the claim breadth and lack of defining features as discussed above, the specification fails to provide an adequate written description of the genus as broadly claimed. Given the lack of written description of the claimed products, any method of using them would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing. See Written Description Requirement guidelines published in Federal Register/ Vol. 66, No.4/ Friday January 5, 2001/Notices: pp. 1099-1111).

Claims 1-15, 19-20, 22-23, 26-28 and 31-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of

decreasing the amount of GAD2 in a plant, decreasing the amount of GABA produced in a plant upon mechanical stimulation, and selecting a transformed plant that exhibits decreased heat shock tolerance, by expressing in a plant a DNA construct comprising a constitutive promoter operably linked in an antisense orientation to a polynucleotide encoding the nonelected GAD2 sequence of SEQ ID NO:4, and while being enabling for a method of increasing the amount of truncated GAD2 in a plant, increasing the amount of GABA produced in a plant, and selecting a transformed plant that exhibits (i) stunted growth and decreased fertility or (ii) taller growth and normal fertility, by expressing in a plant a DNA construct comprising a constitutive promoter operably linked in a sense orientation to a polynucleotide encoding the nonelected GAD2 sequence of SEQ ID NO:4 minus its autoinhibitory calmodulin-binding domain, does not reasonably provide enablement for methods that involve expressing plant GAD enzymes under the control of non-constitutive promoters, or methods that involve expressing other plant GAD enzymes such as the elected plant GAD enzyme of SEQ ID NO:2, or methods that result in other phenotypic effects such as the production of GABA under nonstress conditions of up to about 0.20 mg GABA per gram dry weight. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method for making a transformed plant that selectively increases production of GABA in response to a signal, comprising: incorporating into a plant's genome a DNA construct comprising a non-constitutive promoter operably linked to a polynucleotide that encodes a functional plant GAD enzyme, including a GAD enzyme comprising the amino acid sequence of SEQ ID NO:2 or a sequence having at

least about 60% identity thereto, including a modified GAD enzyme that does not include a functional autoinhibitory calmodulin-binding domain, including a polynucleotide of SEQ ID NO:1 and sequences that hybridize thereto under moderately stringent conditions, to provide a transformed plant; wherein the transformed plant expresses the polynucleotide in response to a signal, and wherein the transformed plant produces GAD enzymes in response to a signal at a rate greater than the rate at which GAD enzymes are produced by a non-transformed plant of the same species under the same conditions. The claims are also drawn to a DNA construct and transformed plants made by said method. The claims are also drawn to a method of making a transformed plant comprising providing a vector comprising a constitutive promoter operably linked to a polynucleotide that encodes a plant GAD enzyme, including a modified GAD enzyme that does not include a functional autoinhibitory calmodulin-binding domain, including a GAD enzyme comprising a sequence having at least about 60% identity to the amino acid sequence of SEQ ID NO:2, and including sequences that hybridize to a polynucleotide of SEQ ID NO:1 under moderately stringent conditions; transforming one or more plants with the vector to provide one or more transformed plants that express the polynucleotide; and selecting a transformed plant that (ii) does not exhibit significant loss of growth characteristics, yield, reproductive function or other morphological or agronomic characteristic compared to a non-transformed plant, including selecting a transformed plant that produces GAD enzymes at a rate substantially greater than the rate at which GAD enzymes are produced by a non-transformed plant of the same species under the same conditions. The claims are also drawn to a transformed plant, including a tobacco plant and a nonsterile plant, comprising a vector comprising a constitutive

promoter operably linked to a polynucleotide that encodes a GAD enzyme, including a plant GAD enzyme, including polynucleotide sequences that hybridize to a polynucleotide of SEQ ID NO:1 under moderately stringent conditions; wherein the plant expresses the polynucleotide and wherein the plant (ii) does not exhibit significant loss of growth characteristics, yield, reproductive function or other morphological or agronomic characteristic compared to a non-transformed plant.

The specification teaches that transgenic *Arabidopsis* plants were made by transforming plants with DNA constructs comprising a constitutive CaMV 35 S promoter operably linked to a polynucleotide encoding either the GAD1 (elected SEQ ID NO:2) or GAD2 (nonelected SEQ ID NO:4) *Arabidopsis* GAD enzymes, said polynucleotide being in a sense orientation, an antisense orientation, or in a sense orientation but lacking the nucleotides encoding the calmodulin binding domain (page 30). However, the specification only discloses the phenotypes of plants transformed with polynucleotides encoding one type of GAD enzyme, the *Arabidopsis* GAD2 (nonelected SEQ ID NO:4) enzyme. Plants transformed with a DNA construct comprising a 35S CaMV promoter operably linked in an antisense orientation to a polynucleotide encoding the nonelected GAD2 sequence of SEQ ID NO:4 had decreased amounts of GAD2, produced decreased amounts of GABA upon mechanical stimulation, and exhibited decreased heat shock tolerance, as compared to nontransformed wild type plants (pages 33-35). Plants transformed with a DNA construct comprising a 35S CaMV promoter operably linked in a sense orientation to a polynucleotide encoding the nonelected GAD2 sequence of SEQ ID NO:4 minus its autoinhibitory calmodulin-binding domain had increased amounts of the truncated GAD2 enzyme, produced increased amounts of GABA, and exhibited either

(i) stunted growth and decreased fertility, or (ii) taller growth and normal fertility, depending on the degree of excess GABA production in the plant (pages 35-37). The specification does not disclose the phenotypes of plants transformed with polynucleotides encoding other GAD enzymes, such as the *Arabidopsis* GAD1 (elected SEQ ID NO:2) enzyme, or GAD enzymes encoded by sequences having at least about 60% identity to SEQ ID NO:1 or by sequences that hybridize to SEQ ID NO:1 under moderately stringent conditions.

The full scope of the claimed invention is not enabled because the effect on transgenic plants of expressing a GAD enzyme, with or without a calmodulin-binding domain, at different levels or at different times or in different locations or under different conditions is unpredictable. The effect is unpredictable because different levels of GAD and its product GABA have different effects on plants. For example, Baum et al. teach that transgenic tobacco plants expressing a mutant petunia GAD enzyme lacking the calmodulin binding domain exhibit severe morphological abnormalities, as well as high GABA and low glutamate levels relative to nontransformed wild type plants, whereas transgenic tobacco plants expressing a full length petunia GAD enzyme exhibited normal morphology, as well as GABA and glutamate levels intermediate relative to nontransformed wild type plants and plants transformed with a mutant petunia GAD enzyme lacking the calmodulin binding domain (EMBO J., 17 June 1996, Vol. 15, No. 12, pages 2988-2996, Applicant's IDS, see page 2990 column 1 first full paragraph and Figure 4). Furthermore, Applicant's own specification teaches that it was known in the art at the time of filing that differential effects (stimulation or inhibition of cell elongation

and plant growth) would occur upon the exogenous application of different concentrations (low versus high) of GABA to plants (page 36 line 28 to page 37 line2).

The effect on transgenic plants of expressing a GAD enzyme is also unpredictable because the level of GAD expression and GAD activity would be affected by multiple variables which include but are not limited to whether the GAD enzyme retained its calmodulin binding domain, the type of promoter and terminator used in the expression vector, the plant species transformed by the expression vector, the type of tissue in which GAD is expressed, the stability of the mRNA transcribed from the GAD coding sequence, the translation efficiency of the mRNA, GAD stability, the availability of glutamate substrate and other substances, such as calcium and calmodulin and PLP, that would affect GAD activity. For example, Turano et al. teach that calcium and calmodulin stimulate GAD activity, and that PLP is required for GAD activity (Plant Physiology, 1998, Vol. 117, pages 1411-1421, see page 1411 first paragraph; page1419 column 1 second full paragraph) Turano et al. also teach that transcriptional events or RNA stability may control the level of GAD activity in leaves, whereas post-translational events may control the level of GAD activity in floral tissue (Plant Physiology, 1998, Vol. 117, pages 1411-1421, see paragraph spanning pages 1419-1420). The full scope of the claimed invention is not enabled because the specification does not provide sufficient guidance for one skilled in the art to determine, without undue experimentation, which combinations of GAD enzymes and non-constitutive promoters would result in a level of GAD expression and/or activity that would produce a specific desired phenotypic effect in plants transformed therewith.

The full scope of the claimed invention is also not enabled because the effect on transgenic plants of expressing a GAD1 enzyme is unpredictable. The effect on transgenic plants of expressing a GAD1 enzyme is unpredictable because GAD1 differs both structurally and functionally from the GAD2 enzyme exemplified in the instant specification. Turano et al. teach that the *Arabidopsis* GAD1 and GAD2 enzymes have 82% amino acid sequence identity, and that recombinant GAD1 and GAD2 expressed in *E. coli* were stimulated 35- and 13- fold respectively by Ca+2/calmodulin (Plant Physiology, 1998, Vol. 117, pages 1411-1421, see column 1 last full paragraph page 1415; page 1417 Table 1; page 1416 column1 first paragraph). In light of the other variables that contribute to the unpredictability of expressing GAD enzymes in general as discussed *supra*, the structural and functional differences between GAD1 and GAD2 enzymes are also considered variables that would contribute to the unpredictability of expressing in a transgenic plant a GAD 1 enzyme as opposed to a GAD2 enzyme. The full scope of the claimed invention is not enabled because the specification does not provide sufficient guidance for one skilled in the art to determine, without undue experimentation, how to express a GAD1 enzyme in a manner that would produce specific phenotypic effects comparable to those produced in plants transformed with constructs comprising GAD2 sequences.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 12, 28, 31, 32, 34, 35, 38 and 40, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 28 and 32 are indefinite in the recitation of "about 60% identity thereto". The metes and bounds of "about 60%" are unclear. Neither the claims nor the specification indicate how much sequence identity would constitute "about 60%". Furthermore, those skilled in the art would interpret "about" differently.

Claim 12, 35 and 40 are indefinite in the recitation of "moderately stringent conditions". It is unclear what type of hybridization conditions would be "moderately" stringent. Neither the claims nor the specification indicate specific hybridization conditions that are "moderately" stringent. Furthermore, those skilled in the art would interpret "moderately" differently.

Claim 34 is indefinite in the recitation of "substantially greater than". The metes and bounds of "substantially greater than" are unclear. Neither the claims nor the specification indicate how much greater the GAD enzyme production rate would have to be in order for the rate to be "substantially" greater than the rate of a non-transformed plant. Furthermore, those skilled in the art would interpret "substantially" differently.

Claims 31 and 38 are indefinite in the recitation of "about 0.20 milligrams GABA per gram dry weight". The metes and bounds of "about 0.20 milligrams" are unclear. Neither the claims nor the specification indicate how much GABA would constitute "about 0.20 milligrams". Furthermore, those skilled in the art would interpret "about" differently.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 14, 22, 37 and 38 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn to progeny of a plant into which a DNA construct has been introduced, but the claims are not limited to progeny that comprise the DNA construct introduced into the parent plant. Due to Mendelian inheritance of genes, a single DNA construct introduced into the parent plant would only be transferred to half of the seeds of that plant. In addition, given that there is no indication of any other distinguishable characteristics of the claimed progeny, it is unclear whether the claimed progeny would be distinguishable from plants that would occur in nature. See *Diamond v. Chakrabarty,* 447 U.S. 303 (1980), *Funk Bros. Seed Co. V. Kalo Inoculant Co.*, 233 U.S. 127 (1948), and *In re Bergey*, 195 USPQ 344, (CCPA). Amendment of the claims to indicate that the progeny comprise the DNA construct introduced into the parent plant would overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Baum et al. (EMBO J., 17 June 1996, Vol. 15, No. 12, pages 2988-2996, Applicant's IDS).

The claims are drawn to a method of making a transformed plant comprising providing a vector comprising a constitutive promoter operably linked to a polynucleotide that encodes a plant GAD enzyme, including a modified GAD enzyme that does not include a functional autoinhibitory calmodulin-binding domain, including a GAD enzyme comprising a sequence having at least about 60% identity to the amino acid sequence of SEQ ID NO:2, and including sequences that hybridize to a polynucleotide of SEQ ID NO:1 under moderately stringent conditions; transforming one or more plants with the vector to provide one or more transformed plants that express the polynucleotide; and selecting a transformed plant that (ii) does not exhibit significant loss of growth characteristics, yield, reproductive function or other morphological or agronomic characteristic compared to a non-transformed plant, including selecting a transformed plant that produces GAD enzymes at a rate substantially greater than the rate at which GAD enzymes are produced by a non-transformed plant of the same species under the same conditions. The claims are also drawn to a transformed plant, including a tobacco plant and a nonsterile plant, comprising a vector comprising a constitutive promoter operably linked to a polynucleotide that encodes a GAD enzyme, including a plant GAD enzyme, including polynucleotide sequences that hybridize to a polynucleotide of SEQ ID NO:1 under moderately stringent conditions; wherein the plant expresses the polynucleotide and wherein the plant (ii) does not exhibit significant loss of growth characteristics, yield, reproductive function or other morphological or agronomic characteristic compared to a non-transformed plant.

Baum et al. teach tobacco plants transformed with a vector comprising a constitutive CaMV 35S promoter operably linked to a polynucleotide that encodes a wild type petunia plant GAD enzyme, and tobacco plants transformed with a vector comprising a constitutive CaMV 35S promoter operably linked to a polynucleotide that encodes a mutant petunia plant GAD enzyme that lacks a calmodulin-binding domain (page 2989 Figures 1 and 2). The plants taught by Baum et al. express the polynucleotide, and they do not exhibit significant loss of growth characteristics, yield, reproductive function or other morphological or agronomic characteristic compared to a non-transformed plant, as evidenced by the normal phenotypic appearance of plants transformed with the wild-type GAD enzyme, and by the failure of Baum et al. to report that plants transformed with the mutant GAD enzyme exhibited a significant loss of yield or other morphological or agronomic characteristic compared to a non-transformed plant (page 2989 Figures 1 and 2; page 2990 Figures 3 and 4; page 2991 Figures 5 and 6;page 2992 Figure 7). The plants transformed with the wild-type GAD enzyme are presumed to be nonsterile, as Baum et al. produced mature flowering transformed plants whose morphology was indistinguishable from that of wild-type plants (page 2989 column 1 first full paragraph and Figure 2). Additionally, the petunia GAD enzyme comprises a sequence having at least about 60% identity to the amino acid sequence of SEQ ID NO:2, and the polynucleotide that encodes a wild type petunia plant GAD enzyme would hybridize to a polynucleotide of SEQ ID NO:1 under moderately stringent conditions, as the polynucleotide that encodes a wild type petunia plant GAD enzyme exhibits significant nucleotide sequence similarity to SEQ ID NO:1 (see the attached comparison of SEQ ID NO:2 and SwissProt Accession No. Q07346, Baum et al., 01 November 1995,

and the attached comparison of SEQ ID NO:1 and GenBank Accession No. L16797, Baum et al., 15 October 1993). Furthermore, the plants transformed with the wild-type GAD enzyme are presumed to a produce GAD enzymes at a rate substantially greater than the rate at which GAD enzymes are produced by a non-transformed plant of the same species under the same conditions, as the plants transformed with the wild-type GAD enzyme exhibit a 10-fold higher specific GAD activity as compared to wild-type plants (page 2993 column 1 first paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15, 19-20, 22-23 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baum et al. (EMBO J., 17 June 1996, Vol. 15, No. 12, pages 2988-2996, Applicant's IDS) in view of McKenzie et al. (Plant Physiology, March 1998, Vol. 116, No.3, pages 969-977).

The claims are drawn to a method for making a transformed plant that selectively increases production of GABA in response to a signal, comprising: incorporating into a plant's genome a DNA construct comprising a non-constitutive promoter operably linked to a polynucleotide that encodes a functional plant GAD enzyme, including a GAD enzyme comprising the amino acid sequence of SEQ ID NO:2 or a sequence having at least about 60% identity thereto, including a modified GAD enzyme that does not include

a functional autoinhibitory domain, including a polynucleotide of SEQ ID NO:1 and sequences that hybridize thereto under moderately stringent conditions, to provide a transformed plant; wherein the transformed plant expresses the polynucleotide in response to a signal. The claims are also drawn to a DNA construct comprising a non-constitutive tissue specific or inducible plant promoter operably linked to a polynucleotide that encodes a functional plant GAD enzyme, a transformed plant that expresses a polynucleotide that encodes a functional plant GAD enzyme, and a transgenic plant cell and plant comprising a DNA construct comprising a non-constitutive promoter operably linked to a polynucleotide that encodes a functional plant GAD enzyme, including a GAD enzyme comprising the amino acid sequence of SEQ ID NO:2 or a sequence having at least about 60% identity thereto.

The teachings of Baum et al. are discussed *supra* in the rejection of claims 31-40 under 35 USC 102.

Baum et al. do not teach the use of a non-constitutive promoter to selectively increase production of GABA in response to a signal.

McKenzie et al. teach the use of a copper controllable root specific promoter to selectively increase the production of the growth affecting compound cytokinin in response to a signal in plants transformed with a DNA construct comprising a non-constitutive promoter operably linked to a polynucleotide encoding isopentenyl transferase (paragraph spanning columns 1-2 page 970). The plants taught by McKenzie et al. exhibited phenotypic effects associated with cytokinin (loss of apical dominance and delayed leaf senescence), but they did not exhibit the morphological abnormalities exhibited by plants transformed with DNA constructs comprising a constitutive promoter

operably linked to a polynucleotide encoding isopentenyl transferase (page 976 paragraph spanning columns 1 and 2).

Given the success of Baum et al. in making transgenic plants that express a GAD enzyme, and given the success of McKenzie et al. in temporally and spatially controlling the expression and phenotypic effect of isopentenyl transferase in transgenic plants, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express in a transgenic plant a functional plant GAD enzyme as taught by Baum et al. using non-constitutive promoter such as the copper controllable root specific promoter taught by McKenzie et al., for the purpose of controlling the phenotypic effect associated with the growth affecting properties of GAD enzyme activity by controlling the time and/or location of GAD enzyme expression, without any surprising or unexplained results. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC

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